selecting a quadruple of radiation wavelengths having minimum error indices.

43. The method of claim 37, said calculating step comprising, correcting said calculated concentrations of said k constituent components as a function of the relative concentrations of the k constituent components.

44. The method of claim 37, said calculating step comprising:

iteratively determining a red blood cell scattering vector for the particular composition of the unaltered whole blood sample being analyzed;

iteratively determining a non-specific scattering vector for the particular composition of the unaltered whole blood sample being analyzed; and

using said red blood cell scattering vector and said non-specific scattering vector to correct said calculated concentrations of said k constituent components.--

(cont B7)

III. RESPONSE

This paper adds new claims 37-44. Claims 1-44 remain in the application and are presented for consideration.

In the Office Action mailed April 26, 1995 ("Office Action 4/26/95"), the third non-final Office Action to be issued in this application, the Examiner, for the first time during the prosecution of this case, objects to the specification under 37

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C.F.R. § 1.117, and rejects claims under 35 U.S.C. § 112, second paragraph. In addition, the Examiner presents four separate bases for rejecting the pending claims under 35 U.S.C. §§ 102 and 103 and under the doctrine of *res judicata*. Applicants respectfully traverse each of the bases for rejecting claims in this application, and present their arguments in more detail in the following sections.

A. <u>The Objection to the Specification is Unfounded</u>

In the objection to the specification (Office Action 4/26/95, at page 2), the Examiner states that she can find no literal support in the specification for the generation of a plurality of substantially monochromatic radiation wavelengths which are divided into two subsets: an absorbance subset of wavelengths and a scattering subset of wavelengths. As a result of this conclusion that there is no literal support for these claimed elements, the Examiner objects to the specification under 37 C.F.R. § 1.117. In light of the comments in the following subsections, Applicants respectfully traverse this rejection.

1. There is no requirement that claim language appear *in ipsis verbis* in the specification.

The Examiner is apparently construing the requirements of 37 C.F.R. § 1.117 to require literal correspondence between the claims and the specification. This is not and never has been the law. In fact, it is well established that "the invention claimed does not have to be described *in ipsis verbis* in order to satisfy the

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description requirement of [35 U.S.C.] § 112." *In re Wertheim*, 541 F.2d 257, 265 (C.C.P.A. 1976).

As pointed out below, the original specification fully satisfies the requirements of all of the sections of 35 U.S.C. § 112, and the Examiner's objection to the specification completely lacks any statutory basis.

2. The original specification provides support for claims 1-36.

The specification of the subject patent application, as originally filed, provides full and complete disclosure of the step of generating a plurality of substantially monochromatic radiation wavelengths, each wavelength of an absorbance subset of the plurality of wavelengths having been selected by their ability to distinguish the constituent components, and each wavelength of a scattering subset of the plurality of wavelengths having been selected to maximize the effects of radiation scattering relative to the effects of absorbance at the scattering wavelengths.

In particular, the original specification describes, at page 9, line 25 through page 10, line 2, that, in one embodiment of the invention, seven wavelengths are generated, six wavelengths having been selected to measure the concentrations of oxyhemoglobin, carboxyhemoglobin, methemoglobin, reduced hemoglobin, sulfhemoglobin and bilirubin, and the seventh wavelength "is chosen from that part of the spectrum where absorbance by bilirubin and each of the five hemoglobin species is as small as possible in comparison with the effects of light scattering." This provides clear support for the generation of seven wavelengths, six forming

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an absorbance subset of wavelengths, and one forming a scattering subset of wavelengths.

In addition, in the original specification, at page 20, lines 24-29, it is explained that

> "n measuring wavelengths are employed to measure k constituent components, with n > k, thereby creating an overdetermined system of equations with respect to the chemical compounds being measured. The n - k extra equations provide a means by which errors due to n - k scattering factors can be compensated."

In other words, in order to measure k components, n measuring wavelengths are employed, k of the n wavelengths forming an absorbance subset of wavelengths, and n-k wavelengths forming a scattering subset of wavelengths.

Next, in the paragraph spanning pages 23 and 24 of the original specification, Embodiments A and B are discussed, each of which require the generation of seven wavelengths. In Embodiment A, six of the seven wavelengths form an absorbance subset of wavelengths, used to measure the concentrations of the six blood components HbO_2, HbCO, Hi, Hb, SHb and br, and the seventh wavelength forms a scattering subset of wavelengths used to correct for light scattering by red blood cells.

As also explained in the same paragraph, in Embodiment B, five of the seven wavelengths form an absorbance subset of wavelengths used to measure the concentrations of the five blood components HbO_2, HbCO, Hi, Hb and br, and two of the seven wavelengths form a scattering subset of wavelengths used to correct for nonspecific light scattering, and to correct for light scattering by red blood cells.

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Finally, in the paragraph spanning pages 34 and 35, Embodiment C is described which uses eight wavelengths, six of the eight wavelengths forming an absorbance subset of wavelengths used to measure the concentrations of the six blood components HbO_2, HbCO, Hi, Hb, SHb and br, and the seventh and eighth wavelengths forming a scattering subset of wavelengths used to correct for the effects of red blood cell scattering and nonspecific scattering.

Thus, although the original specification (other than the original claims), never used the "subset" terminology, the original specification provided clear support for the generation of a plurality of wavelengths including an absorbance subset of wavelengths and a scattering subset of wavelengths.

3. The amendments to the specification now provide literal support for claims 1-36.

Notwithstanding that there is no statutory basis to require Applicants to amend the specification to include the literal claim language of claims 1-36 in the specification, Applicants, in the interest of advancing this case to allowance, have amended the specification to do just that.

In particular, the Summary of the Invention has been amended to add a paraphrase of each of claims 1-36, and portions of the specification at pages 9, 16, 20, 23 and 35 have been amended to reflect the "subset" language appearing in the original claims.

No new matter has been added to the specification because each of the amendments to the specification are fully and completely supported by the claims contained in the application as originally filed. It is well established that the originally filed claims may

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be considered as part of the original disclosure of the application. *See e.g. McBride V. Teeple*, 109 F.2d 789, 796 (C.C.P.A. 1940).

* * *

In light of the foregoing comments and amendments to the specification, withdrawal of the objection to the specification is respectfully requested.

B. The Rejection of Claims Under § 112, Second Paragraph is Wrong

The Examiner rejects claims 1-36 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. In particular, the Examiner is confused by the fact that the absorbance subset of wavelengths, and the various dimensional aspects of the invention, are all selected to minimize radiation scattering, whereas the scattering subset of wavelengths is selected to maximize radiation scattering relative to absorbance at the scattering wavelengths. Applicants respectfully traverse this rejection because the claim language is internally consistent, unambiguous and clear, and accurately describes the invention.

In particular, as explained in the Section III.A above, the present invention generates a plurality of wavelengths which include an absorbance subset of wavelengths, and a distinct scattering subset of wavelengths. As recited in the claims, and as explained in detail in the specification, each member of the absorbance subset of wavelengths has been selected by its ability to distinguish the constituent components under consideration,

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whereas each member of the scattering subset of wavelengths has been selected to maximize radiation scattering relative to the effects of absorbance in order to provide a means to compensate errors due to scattering factors in unaltered whole blood.

Specifically, Applicants refer the Examiner to the above discussion in Section III.A.2 regarding the description of the absorbance subset and scattering subset in the original specification at pages 9-10, 20-21, 23-24 and 34-35.

Thus, the existence of an absorbance subset of wavelengths, the members of which are selected to maximize absorbance relative to radiation scattering, along with a scattering subset of wavelengths, the members of which are selected to maximize the effects of scattering relative to absorbance, is completely compatible.

The Examiner cites page 14, lines 27-34 of the original specification in support of the misperception that "the main purpose of Applicants' device is to minimize the effects of radiation scattering," (Office Action 4/26/95, at 4). This represents a fundamental misunderstanding of the invention, and a complete ignorance of large portions of the written description which relate to Applicants' invention. The portion of the specification cited by the Examiner appears in a section of the specification entitled "Optical Geometry, Other Apparatus, and Mode of Operation," and deals with the dimensional aspects of the invention (for example, sample depth, detector distance and detector area). The portion cited by the Examiner has nothing

whatsoever to do with the particular wavelengths that are used to irradiate the unaltered whole blood sample. As explained above, the radiation wavelengths selected in accordance with Applicants' invention include some that are selected to maximize absorbance and minimize scattering, and some that are selected to maximize scattering relative to absorbance.

* * *

In light of the foregoing comments, Applicants respectfully request the Examiner to withdraw the rejection of the claims under 35 U.S.C. § 112, second paragraph.

C. <u>The Rejections Based on Prior Art are Unfounded</u>

1. The ten declarations strongly support patentability.

Filed herewith are five declarations, making a total of ten declarations in this case including, two declarations filed with the Amendment on March 25, 1994, and three declarations filed with the Request for Reconsideration on December 15, 1994. Reference will be made herein to each of these ten declarations.

For completeness, the following table presents each of the ten declarations, the date they were signed, and their form of citation within this paper.

Declaration	Citation Form
Declaration of Joseph M. Schmitt Under 37 C.F.R. § 1.132, signed February 25, 1994	"Schmitt 2/25/94, ¶ ___"

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Declaration of Roland N. Pittman Under 37 C.F.R. § 1.132, signed February 28, 1994	"Pittman, ¶ ___"
Declaration of Gert E. Nilsson Under 37 C.F.R. § 1.132, signed December 8, 1994	"Nilsson, ¶ ___"
Declaration of Per Åke Öberg Under 37 C.F.R. § 1.132, signed December 12, 1994	"Öberg, ¶ ___"
Declaration of A. P. Shepherd Under 37 C.F.R. § 1.132, signed December 12, 1994	"Shepherd 12/12/94, ¶ ___"
Supplemental Declaration of Joseph M. Schmitt Under 37 C.F.R. § 1.132, signed July 10, 1995	"Schmitt 7/10/95, ¶ ___"
Declaration of Charles F. Mountain Under 37 C.F.R. § 1.132, signed July 6, 1995	"Mountain, ¶ ___"
Declaration of Thomas Scecina Under 37 C.F.R. § 1.132, signed July 13, 1995	"Scecina, ¶ ___"
Supplemental Declaration of A. P. Shepherd Under 37 C.F.R. § 1.132, signed August 14, 1995	"Shepherd 8/14/95, ¶ ___"
Declaration of A. P. Shepherd and John M. Steinke Under 37 C.F.R. § 1.131, signed October 4, 1995	"Shepherd and Steinke, ¶___"

These declarations relate to the issues of patentability in light of the prior art, and significant secondary considerations including licensing of the invention, commercial success, failure of others in the field to arrive at the present invention, despite long felt need, and unexpected results. These declarations, which will be cited throughout the rest of these remarks, strongly support the patentability of the claims pending in this application.

2. Secondary considerations strongly support patentability.

a. Commercial success, including licensing the invention, supports patentability.

The negotiation for license with Instrumentation Laboratory Company reported in the paper filed December 15, 1994 (*also see*, Shepherd 12/12/94, ¶ 7), has been successfully completed. Instrumentation Laboratory Company now holds a license to the patent and know-how rights owned by A-VOX Systems, Inc. (the exclusive licensee of the patent owner, The University of Texas System) relating to the invention described in the subject patent application. Instrumentation Laboratory Company has the exclusive right to incorporate these patent and know-how rights in the restricted field of non-portable, bench-type products used to measure one or more of the following in unaltered whole blood: bilirubin concentration, total hemoglobin concentration, relative oxyhemoglobin concentration, relative deoxyhemoglobin concentration, relative carboxyhemoglobin concentration, relative methemoglobin concentration or relative sulfhemoglobin concentration. Patent know-how rights are expressly defined in the license to include the information and discoveries described in the present patent application (U.S. Patent Application Serial No. 07/953,680). Shepherd 8/14/95, ¶ 6.

That license specifies a license initiation fee of $50,000, with a minimum royalty over the life of the agreement of over $1,000,000. If sales of the licensed product reach projected

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levels, the total royalty over the life of the agreement will exceed $11,000,000. Shepherd 8/14/95, ¶ 7.

The Office Action 4/26/95, at page 28 indicated that the first Shepherd declaration (Shepherd 12/12/94) was deemed by the Examiner to be "mute" because the Declaration allegedly did not make clear what the commercial success is attributed to.

Since Examiner Hantis was present at a demonstration of the AVOXimeter 1000 on January 19,1994, and since a brochure completely describing the functions of that product was attached to Dr. Shepherd's declaration of 12/94, it is unreasonable for the Examiner to imply, without any support, that the commercial success was somehow due to unclaimed features. In addition, as explained in Dr. Shepherd's supplemental declaration, claim 1 of the present application covers the core functions of the AVOXimeter 1000, and, other than displaying the calculated concentrations, the AVOXimeter 1000 performs no other functions of consequence. Shepherd 8/14/95, ¶ 2. In addition, the subject matter of the license between A-VOX Systems, Inc. and Instrumentation Laboratory Company is the very invention described in the subject patent application. Thus, the required nexus exists between the commercialization of the present invention and the claimed invention because at least claim 1 of the present application covers the entire AVOXimeter 1000, and because the licensed technology is the very technology described in the subject patent application.

In such a situation, "*prima facia* evidence of nexus is established if there was commercial success and if the invention

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disclosed in the patent was that which was commercially successful." *Ryko Manufacturing Co. v Nu-Star, Inc.*, 950 F.2d 714, 719 (Fed. Cir. 1991); *see also, Dmaco Corp. v F. Von Langsdorff Licensing Co. Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir.) *cert denied*, 488 U.S. 956 (1988).

The AVOXimeter 1000 continues to enjoy remarkable commercial success. From the beginning of sales in 1993, through the first six months of 1995, over 185 units have been sold, which have resulted in accounts receivable of over $1,400,000 for the oximeter and disposable cuvettes. Shepherd 8/14/95 ¶¶ 3-5. The sales in 1994 represented a 250% increase over the sales in 1993, and the sales for the first six months of 1995 represent over 64% of the receivables for the entirety of 1994, indicating the possibility of a substantial increase in 1995 over 1994.

Thus, it is clear that there are the beginnings of significant sales of products embodying the invention, without distributors and using only direct mail advertising. Shepherd 8/14/95, ¶¶ 3-5. These sales figures and the dramatic increase over a very short time are indicative of the beginnings of a "rush to the invention [that is] probative of non obviousness." *Nicola v Peterson*, 580 F.2d 898, 914 (6th Cir. 1978) (opinion by Judge Markey, then Chief Judge of the C.C.P.A.).

Such evidence of secondary considerations has great utility in a patentability determination, *Grahm v. John Deere Co.*, 383 U.S. 1, 17-18 (1966), and in fact, "requires a finding of nonobviousness if the matter can be otherwise doubtful," *In re Sernaker*, 702 F.2d

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989, 996 (Fed. Cir. 1983) (nonobviousness shown from license from patent not yet issued). In addition, when evidence is submitted to rebut an Examiner's contention of obviousness, the Examiner must start over. Facts established by rebuttal evidence must be evaluated along with facts on which the earlier conclusion of obviousness is reached, not against the conclusion itself. In other words, it is error to review rebuttal evidence solely for its "knockdown ability." *In re Piasecki*, 745 F.2d 1468, 1472-73 (Fed. Cir. 1984); *In re Rinehart*, 531 F.2d 1048, 1052 (C.C.P.A. 1976).

Applicants respectfully assert that this evidence shows remarkable commercial success, which includes not only significant sales of the product embodying the invention, but also the licensing of the invention for substantial royalties, even before the patent application has issued. This evidence of commercial success is sufficient to overcome any *prima facia* case of obviousness that may have been established by the Examiner.

b. Failure of others in the industry, long felt need, and unexpected results all support patentability.

It is well established that the failure of others in the field to come up with the invention, despite the presence of a long felt need, is strong evidence of non-obviousness *In re Dow Chemical Corp.*, 837 F.2d 469, 472 (Fed. Cir. 1988) ("Recognition of need, and difficulties encountered by those skilled in the field are classical indicia of nonobviousness."). Such is the case with the present invention.

Specifically, filed herewith are the declarations of Charles F. Mountain and Thomas Scecina, each an expert in the field of blood spectophotometery, and each a developer of blood co-oximeters for major manufacturers.

Mr. Mountain is the co-inventor of U.S. Patent No. 4,134,678 to Brown *et al.*, which is one of the patents applied by the Examiner in the subject Office Action to reject claims. Mountain, ¶ 3. During the five year period preceding the filing of the Brown *et al.* patent application, Mr. Mountain's employer, Instrumentation Laboratory Company, had a team of highly qualified technical experts attempt to design a spectrophotometric device capable of measuring multiple hemoglobin species. One approach taken was to attempt to measure multiple hemoglobin species in unaltered whole blood because this approach offered significant commercial advantages over a system requiring hemolysis. Mountain, ¶ 4.

These advantages included: (1) lower manufacturing costs, (2) simplification of mechanical and fluidics components by eliminating the processes of hemolysis and dilution, (3) simplification of the calibration of total hemoglobin measurement by eliminating sample dilution, (4) faster analysis, and (5) greater ease of integration with a system for blood gas analysis. *Id.*

Mr. Mountain was a member of the design team responsible for developing the spectrophotometric device, and was specifically aware of the teachings of Anderson and Sekelj, *Phys. Medic Bio*, Vol. 12, 2:173-174, 1967. Mountain ¶ 5.

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Despite years of effort that included numerous experiments with unaltered whole blood in various optical designs and strategies, the Instrumentation Laboratory design team failed in its attempt to devise a means of measuring multiple hemoglobin species directly in unaltered whole blood. Mountain, ¶¶ 7-9. The effort to make measurements directly in nonhemolyzed blood was abandoned at Instrumentation Laboratory, and the spectrophotometric device disclosed in the Brown *et al.* patent was developed. That device, consistent with the disclosure of the Brown *et al.* patent, requires hemolysis prior to the spectrophotometric measurement of multiple hemoglobin species. Mountain, ¶¶ 10-11.

In addition, Mr. Thomas Scecina, who was employed by Ciba Corning from 1973 to 1995, also attempted, with a "team of highly qualified scientists and instrument designers," at Ciba Corning to develop a method for measuring multiple hemoglobin species in unaltered whole blood. Scecina, ¶ 5. The reason for attempting such development was that such an instrument would be simpler, faster, and less expensive to manufacture than co-oximeters that hemolyze each blood sample before analyzing it spectrophotometrically. Mr. Secina concluded that the need for such an instrument was quite evident and longstanding. Scecina, ¶ 5.

Despite the desirability and longstanding need for such a design, Mr. Scecina's design team abandoned their effort to develop the instrument because nothing in their experiments or in the literature indicated that such measurements were feasible at the

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required accuracies due to the complex optical properties of unaltered whole blood, and because their experiments indicated that making measurements on unaltered whole blood might be risky and unreliable because the optical behavior of unaltered whole blood was so unpredictable from one sample to the next. Scecina, ¶ 7.

Thus, the development effort at Ciba Corning was also abandoned. Scecina, ¶ 7-8.

In addition, each gentleman finds the present invention to produce remarkable and surprising results. Specifically, with reference to Table IV on page 40 of the present application, Mr. Mountain finds it to be "an astonishing accomplishment" that the present invention can make measurements in unaltered whole blood that agree, as closely as they do, with those in hemolyzed blood. Mountain, ¶ 8. Mr. Scecina, like Mr. Mountain, has reviewed the present patent application, including Table IV on page 40, and finds it "quite surprising that the present invention can make measurements in unaltered whole blood that agree so well with those in hemolyzed blood." Scecina, ¶ 12.

Applicants respectfully assert that the existence of long-felt need, the failure of those in the industry to arrive at the invention despite this long-felt need, and the statements by two experienced designers in the industry who work for two of the four major suppliers of products in the field, finding the results accomplished by the invention to be "astonishing" and "surprising," exhibits strong evidence of secondary considerations, and strongly supports the patentability of the presently claimed invention.

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In the light of these strong secondary considerations, the patentability of the present invention is clear. Specifically, this evidence shows remarkable commercial success, including not only significant sales of the product embodying the invention, but also the licensing of the invention for substantial royalties, even before the patent application is issued. In addition, the evidence shows the existence of long-felt need, the failure of those in the industry to arrive at the invention despite this long-felt need, and the surprising results achieved by the invention.

This evidence of secondary considerations is sufficient to overcome any *prima facia* case of obviousness that may have been established by the Examiner.

3. The rejections based on Anderson *et al.* are wrong.

The Examiner rejects claims 1, 10, 20-24, 26-27 and 34-36 under 35 U.S.C §102 as being anticipated by Anderson and Sekelj, "Light-Absorbing and Scattering Properties of Non-Haemolyzed Blood," *Phys. Med. Bio.*, Vol. 12, 2:173-184, 1967 ("Anderson *et al.*"), rejects claims 2-9, 11-19, 25 and 28-33 under 35 U.S.C. §103 as being obvious in view of Anderson *et al.*, and rejects claims 1-36 under 35 U.S.C §103 as being unpatentable over the combination of Anderson *et al.* and Brown *et al.*, U.S. Patent No. 4,134,678 ("Brown *et al.*"). Applicants respectfully traverse each of these rejections. The following subsections are dedicated to a discussion of the Anderson *et al.* reference, and The Brown *et al.* reference is discussed below in Section III.C.5.

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a. Anderson *et al.* test altered blood of known composition.

Independent claim 1 of the present application requires the determination of "concentrations of a plurality of constituent components of unaltered whole blood of unknown composition," (emphasis added). The Examiner believes that Anderson *et al.* performed measurements of unaltered whole blood of unknown composition. Office Action 4/26/95, at page 7. Such is not the case.

The second paragraph on page 177 of Anderson *et al.* states (with added emphasis): "Fully oxygenated nonhaemolysed red cells suspended in isotonic saline were studied. . . ." Nowhere in the disclosure of Anderson *et al.* is there any teaching of measuring unaltered whole blood, as required by the presently claimed invention. The Examiner has come forward with nothing more than conclusions that such teaching exists, without citation to any relevant text of Anderson *et al.*, despite numerous requests by Applicants for such specific citation.

Before suspending nonhemolyzed red blood cells in isotonic saline, Anderson *et al.* must first separate the red blood cells from the other components of whole blood, thus altering the blood sample. This effectively eliminates many of the contributors to light scattering mentioned in the third paragraph on page 7 of the present application, and discussed below in detail in Section III.C.3.c. Moreover, by using "fully oxygenated" red cells, the samples used by Anderson *et al.* are of known composition, *i.e.*, oxyhemoglobin (also referred to as HbO_2 in the present

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application). No other hemoglobin components (deoxy-, carboxy-, met- or sulfhemoglobin or bilirubin), are present in the samples measured by Anderson *et al.*

Therefore, contrary to the Examiner's interpretation of Anderson *et al.*, Anderson *et al.* measure altered whole blood of known composition. Pittman, ¶ 11; Schmitt 2/25/94, ¶ 11; Nilsson, ¶ 16; Öberg, ¶ 16; Schmitt 7/10/95, ¶6.

b. Anderson *et al.* do not measure concentrations of any components of unaltered whole blood.

As emphasized in the previous section, the presently claimed invention measures "concentrations of a plurality of constituent components of unaltered whole blood of unknown composition." In contrast, also as noted above, each of the measurements taken by Anderson *et al.* are taken on "red-cell suspensions," which, in accordance with the second paragraph on page 177 of Anderson *et al.*, means that only fully oxygenated non-hemolyzed red cells suspended in saline were studied.

In fact, the legends of each of the graphs depicted in the figures of the Anderson *et al.* article, with the exception of Figure 5, expressly state that what was being studied were "red cell suspensions," and it is quite likely that the measurements depicted in Figure 5 were also taken from red-cell suspensions. Schmitt 7/10/95, ¶ 6.

Although Anderson *et al.* disclose that the difference in total optical attenuation before and after hemolysis of a particular red-cell suspension in saline is an estimate of the magnitude of light scattering before that particular blood suspension was hemolyzed

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(Schmitt 7/10/95, ¶4), there is absolutely no disclosure in Anderson *et al.* of measuring unaltered whole blood of unknown composition for any purpose. The Examiner's conclusion to the contrary is simply pure conjecture, without citation to any relevant portion of Anderson *et al.*.

That Anderson *et al.* does not ever measure unaltered whole blood is further emphasized by the fact that curve C in Figure 6 of Anderson *et al.* indicates that the magnitude of light scattering varies with total hemoglobin concentration. Thus, the only way to use Anderson *et al.* to "correct" for the effects of scattering when measuring a sample of unaltered whole blood, as contended by the Examiner (Office Action 4/26/95 at page 6), is first to measure the total hemoglobin concentration of the sample under test by some independent method. This prior measurement would thus render any sort of measurement by the apparatus disclosed in Anderson *et al.* completely superfluous, and thus useless. In addition, this prior measurement would render the sample of "known" composition, contrary to the requirements of the presently claimed invention. Schmitt 7/10/95, ¶4.

Moreover, it is clear that Anderson *et al.* do not perform any tests on unaltered whole blood because Anderson *et al.*, while measuring the scattering characteristics of red blood cells suspended in saline, do not measure the scattering effects present in unaltered whole blood, which are measured by the present invention. Such unaltered whole blood includes red blood cells suspended in plasma, and the plasma includes many things other than

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red blood cells. Schmitt 7/10/95, ¶ 7. The following section, with its subsections, presents, why Anderson *et al.* do not, and in fact are incapable of, making meaningful measurements of the concentrations of the constituent components of unaltered whole blood, because Anderson *et al.* do not adequately take into account any of the scattering factors present in unaltered whole blood -- scattering factors that are accommodated only by the present invention.

c. Anderson *et al.* do not contemplate scattering correction.

Independent claim 1 of the present application requires the generation of a plurality of radiation wavelengths, the plurality of wavelengths including an absorbance subset that has been selected by its ability to distinguish the constituent components of unaltered whole blood of unknown composition, and having been selected to minimize the effects of radiation scattering and to maximize radiation absorbance by these constituent components. The plurality of wavelengths also includes a scattering subset of wavelengths that has been selected to maximize the effects of scattering by unaltered whole blood relative to the effects of radiation absorbance by unaltered whole blood.

Claim 1 also requires the calculation of the concentrations of the plurality of constituent components of the sample of unaltered whole blood, corrected for the effects of radiation scattering, as a function of detected intensities of the radiation wavelengths of the absorbance subset and of the scattering subset, after passing

through the sample. Dependent claims 20-36 expand on the details of correction for the effects of radiation scattering.

The Examiner relies on the first paragraph from page 180 of Anderson *et al.* for the proposition that Anderson *et al.* allegedly contemplate correction for scattering. Office Action 4/26/95, at 4.

Applicants believe this conclusion by Anderson *et al.* to be fundamentally incorrect, and believe that it may have misled the Examiner to thinking that Anderson *et al.* can accurately deduce the magnitude of light scattering produced by an unknown sample of whole blood from measured optical density values and known extinction coefficients of the hemoglobin species under consideration.

The relevant statement on page 180 of Anderson *et al.* shows that key aspects of the presently claimed invention were completely unknown to Anderson *et al.* Specifically, the statement is completely false since it does not account for:

- the sample-to-sample variation in light scattering in whole blood due to the eight factors described on page 7, paragraph 3 of the present application; or
- the hemoglobin species-dependence of the scattering vectors described on page 7, paragraph 2 of the present application; or

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- the wavelength dependence of the scattering vectors described on page 7, paragraph 1 of the present application; or
- the fact that there are actually at least two independent scattering vectors to be found when whole blood is illuminated, as described on pages 20-30 of the present application.

In accordance with the presently claimed invention, it is the generation of the scattering subset of wavelengths, in addition to the absorbance subset of wavelengths, that permits the presently claimed invention to correct for errors introduced in the determination of the concentrations of the constituent components of unaltered whole blood of unknown composition. Such correction is nowhere contemplated by Anderson *et al.*, as explained in more detail in the following subsections.

(1) Light scattering in unaltered whole blood samples is unpredictable from one sample to another.

As mentioned in the third paragraph on page 7 of the present application, there are at least eight uncontrolled factors identified that make light scattering in whole blood samples unpredictable from one sample to another. These are: 1) the different plasma protein concentrations that determine the refractive index of plasma in one sample versus another; 2) the aggregation of red blood cells in the sample; 3) the different hemoglobin concentrations inside the red cells that alter their refractive index; 4) the size and shape of the red blood cells; 5)

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chylomicrons or other light-scattering lipid particles; 6) cell fragments; 7) microscopic clots; and 8) light-sieving effects of sedimented red blood cells. Schmitt 2/25/94, ¶¶ 10, 12, 14; Pittman, ¶¶ 10, 12, 14; Öberg, ¶ 11; Nilsson, ¶ 11; Schmitt 7/10/95, ¶¶ 7-14.

In trying to back-calculate hemoglobin concentrations from measured optical densities of whole blood for an unknown sample of whole blood, one cannot first adjust the parameters in Twersky's equation (the equation used by Anderson *et al.*) to fit the data and then turn around and subtract off the scattering term to determine the part due to absorbance by hemoglobin, yet this is what would have to be done even to attempt to apply Twersky's theory in the manner suggested by the Examiner. Schmitt 2/25/94, ¶ 9; Pittman, ¶ 9; Nilsson, ¶ 12; Öberg, ¶ 12. Furthermore, the Twersky formalism used by Anderson *et al.* describes "ideal" whole blood, and does not even include provisions for dealing with red cell aggregation, chylomicrons, cell fragments, and other uncontrolled factors that cause light scattering in real whole blood samples. Schmitt 2/25/94, ¶ 10; Pittman, ¶ 10; Nilsson, ¶ 11; Öberg, ¶ 11. Moreover, as mentioned above in Section III.C.3.a., Anderson *et al.* perform measurements on "ideal" whole blood in the form of oxygenated red cells suspended in isotonic saline.

(2) Light scattering in unaltered whole blood samples depends in a complicated way on the particular hemoglobin species present in the sample under consideration.

In the second paragraph on page 7 of the present application, it is pointed out that the total contribution to the optical

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absorbance of whole blood due to light scattering depends in a complicated way on the actual hemoglobin species present in the sample under consideration. For example, the sample may be comprised purely of oxyhemoglobin or 50% oxyhemoglobin and 50% carboxyhemoglobin, or the sample may be comprised of any combination of the possible hemoglobin species. A naive reading of Anderson *et al.* (namely that the contribution to unaltered whole blood's optical absorbance which is due only to light scattering is determined by path length, total hemoglobin concentration, and detecting geometry) would not allow for the dependence of light scattering on the particular hemoglobin species present in the given sample.

The presently claimed invention, by generating a scattering subset in addition to an absorbance subset of wavelengths (claim 1), makes a quantitative correction for the light scattering of each unknown blood sample as a function of the particular hemoglobin species it contains (also see Figures 4 and 5 of the present application, and supporting text). This correction is expressly included in claims 21, 24 and 27 (and claims 22, 25 and 28-33 dependent therefrom). The passage cited by the Examiner from page 180 of Anderson *et al.* demonstrates that Anderson *et al.* were completely unaware of the necessity of having a hemoglobin-species-dependent scattering vector.

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(3) Light scattering in unaltered whole blood depends in a complicated way on the wavelength of the impinging light.

In the first paragraph on page 7 of the present application, it is pointed out that the total contribution to the optical absorbance of whole blood due to light scattering depends in a complicated way on the wavelength of the impinging light. In the passage cited by the Examiner from page 180 of Anderson *et al.*, it is stated that "scattering remains the same for this sample depth and haemoglobin content when wavelength is varied." This assertion is patently false as the data of Pittman clearly shows. *See*, Figure 3 of the present application; Nilsson, ¶ 11; Öberg, ¶ 11. In contrast to this misconception of Anderson *et al.*, the present invention makes a quantitative correction for the light scattering of each unknown blood sample (claim 1), specifically by employing scattering vectors that vary with wavelength (claims 34, 35 and 36). The passage cited by the Examiner demonstrates that Anderson *et al.* were completely unaware of the necessity or utility of using wavelength-dependent scattering vectors.

(4) There are actually at least two independent scattering vectors to be found when whole unaltered blood is illuminated.

Pages 20-30 of the present application describe both a red blood cell scattering vector and a nonspecific scattering vector. Claims 20, 23 and 26 (and claims 21, 22, 24, 25 and 27-36 dependent therefrom) are specifically directed to these features. Both vectors are important in making accurate measurements of the concentrations of hemoglobin species in unaltered whole blood.

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There is no hint of two or more forms of scattering in Anderson *et al.*, or in Twersky's theory used by Anderson *et al.* Therefore, the innovation of these two independent scattering vectors as disclosed and claimed in the present application is original and could not have been deduced from Anderson *et al.*

* * *

In rejecting claims 1, 10, 20-24, 26-27 and 34-36 under 35 U.S.C. § 102(b) as anticipated by Anderson *et al.*, the Examiner asserts that "Anderson inherently has correction" for light scattering (Office Action 4/26/95, at p. 6). The foregoing discussion demonstrates that the only "correction" that Anderson *et al.* have is merely a fixed quantity that fails to take into account the eight or more uncontrolled factors that make the magnitude of light scattering unpredictable from one sample of whole blood to the next, that fails to contemplate a scattering subset of wavelengths to accommodate these uncontrolled factors (claim 1), that fails to treat the wavelength-dependence of the light scattering (claims 34, 35 and 36), that does not account for the variation of the magnitude of light scattering from one blood sample to another (claims 22 and 25), that does not account for the dependence of the magnitude of light scattering on the particular hemoglobin species present in the sample (claims 21, 22, 24, 25 and 27-33), and that does not include either of the scattering vectors of the presently claimed invention (claims 20-36). For this reason alone, Applicants respectfully request the Examiner to withdraw the

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rejection of claims 1, 10, 20-24, 26-27 and 34-36 as being anticipated by Anderson *et al*.

4. The rejections based on Curtis are unfounded.

On pages 8 and 9 of the Office Action of 4/26/95, the Examiner concludes that Curtis, U.S. Patent No. 5,064,282 ("Curtis"), either anticipates, or renders obvious, each of claims 1-36. Applicants respectfully traverse all rejections based on Curtis

a. Curtis is not prior art.

On page 8 of the subject Office Action, the Examiner includes an incomplete, conclusory statement as to what is disclosed by Curtis.

Applicants readily admit that Curtis discloses the generation of a plurality of wavelengths, the irradiating of a blood sample (albeit, a hemolyzed blood sample) with the plurality of wavelengths, detecting the intensity of the wavelengths after passing through the sample, and the calculation of the amount of hemoglobin in the sample, as a function of the wavelengths. However, well prior to September 26, 1989 (the earliest possible date that the Curtis reference can be prior art), Applicants reduced these very features to practice. This eliminates Curtis as a prior art reference.

In particular, filed herewith is a declaration signed by each of the Applicants under 37 C.F.R. § 1.131, averring that, with respect to so much of the subject matter recited in claims 1-36 presently pending in this case as is shown by the Curtis reference, Applicants reduced that subject matter to practice in the United

States well prior to September 26, 1989. Shepherd and Steinke, ¶ 3.

In particular, a written disclosure of the invention was provided to a Mr. George F. Sedivy, of Waters Instruments, Inc., as an attachment to a confidentiality agreement (Shepherd and Steinke, Exhibit 1), prior to September 26, 1989. Substantially contemporaneous with the signing of the confidentiality agreement, Mr. Sedivy observed the system in operation embodying the relevant disclosure of Curtis. Shepherd and Steinke, ¶¶ 5-6, Exhibit 1.

That system generated four wavelengths which were used to measure four different hemoglobin species of whole blood: oxy-, deoxy-, carboxy- and met-hemoglobin. Shepherd and Steinke, ¶ 4, Exhibit 1. The system included a detector for measuring the intensities of the wavelengths after passing through the sample, and a computer for solving four simultaneous linear equations to compute the concentrations of each of the four species being measured. *Id.*

After the system was constructed, it was tested prior to September 26, 1989, to prove to the satisfaction of Drs. Shepherd and Steinke that the system produced satisfactory measurements of the percentages of the hemoglobin species under consideration. Shepherd and Steinke, ¶ 7. Drs. Shepherd and Steinke also confirmed that their system, which was constructed prior to September 26, 1989, formed the basis for U.S. Patent Application Serial No. 07/313,911, filed February 23, 1989. Shepherd and

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Steinke, ¶ 8. That application is the parent of the present continuation-in-part application.

Thus, the present inventors reduced to practice so much of the subject matter as is shown by Curtis, well prior to September 26, 1989. Curtis thus cannot be prior art. *In re Stempel*, 241 F.2d 775, 759 (C.C.P.A. 1957) (to eliminate a reference as prior art under Rule 131, "all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference.").

Although the prior reduction to practice did not include the generation of a scattering subset of wavelengths, and the calculation of concentrations of components corrected for the effects of scattering as a function of the scattering subset of wavelengths, and such is not disclosed in parent application Serial No. 07/313,911, there is no disclosure in Curtis of this concept either. Thus, in accordance with the law of Rule 131 set forth in *Stempel*, Applicants' Rule 131 declaration is effective to overcome Curtis' prior art.

However, as explained in the following subsections, even if Curtis were prior art, it cannot be used to render the presently claimed invention unpatentable.

b. Curtis alters the blood sample by hemolysis.

The Examiner states that Curtis is "an unaltered whole blood analysis system," (Office Action 4/26/95, at 9). However, this is not the case because Curtis hemolyzes the blood sample before

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measurement. Curtis states explicitly that prior hemolysis of the sample is a necessary and an essential step in his measurement method.

Specifically, Curtis, at column 2, line 4, states, "The only reagent required is a lysing agent which breaks up the erythrocytes to release the hemoglobin." Similarly, at column 5, line 45, Curtis states ". . . the only reagent required is saponin, a natural substance which acts as a lysing agent and breaks up the erythrocytes to release hemoglobin." Öberg, ¶ 6; Nilsson, ¶ 6.

By contrast, the presently claimed invention makes multiple spectrophotometric measurements directly in "unaltered whole blood," without hemolysis or other conditioning (claim 1).

Although the Examiner concludes that "minimization of radiation scattering are [sic] disclosed by Curtis," (Office Action 4/26/95, at 8), it is clear from the disclosure of Curtis that Curtis does not disclose minimization of radiation scattering by any means other than hemolysis. Öberg, ¶ 8; Nilsson, ¶ 8; Schmitt 7/10/95, ¶ 20. Moreover, because the method of Curtis requires hemolysis, Curtis gives no clues whatsoever as to how one would make meaningful measurements in the presence of the intense light scattering produced by unaltered whole blood -- measurements that only the presently claimed invention permits.

c. Curtis does not contemplate a scattering correction for unaltered whole blood.

At page 8 of the subject Office Action, the Examiner erroneously concludes that Curtis renders obvious the selection of

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radiation wavelengths recited in claims 11-19 and 29-33. Applicants respectfully traverse this rejection.

Curtis selects two wavelengths for the purpose of measuring total hemoglobin concentration (Curtis, Abstract). However, contrary to the Examiner's conclusion, Curtis' method of selecting these wavelengths is completely different from that of the presently claimed invention.

Specifically, Curtis states:

> Two absorbance measurements are made, the first at a wavelength at which the absorbance of oxyhemoglobin and deoxyhemoglobin are approximately equal, near an isobestic point, and a second measurement at which these components absorb substantially no light.

Curtis, Abstract, lines 8-13; *also see* column 4, lines 21-30; *accord* Öberg, ¶ 13; Nilsson, ¶ 13; Schmitt 7/10/95, ¶ 21.

Thus, while Curtis contemplates selecting radiation wavelengths based upon absorbance criteria, there is absolutely no disclosure or suggestion in Curtis of selecting an absorbance subset of wavelengths "by their ability to distinguish the constituent components and . . . to minimize the effects of radiation scattering and to maximize radiation absorbance by said constituent components," as expressly required by independent claim 1. Further, there is absolutely no disclosure or suggestion in Curtis of a scattering subset of wavelengths that has been "selected to maximize the effects of radiation scattering by unaltered whole blood relative to the effects of radiation absorbance by unaltered whole blood," also as required by independent claim 1. For this reason alone, dependent claims 11-19

and 29-33 should not be considered obvious in light of the teachings of Curtis.

In addition, there is absolutely no disclosure or suggestion of the selection of radiation wavelengths based on the minimization of error indices that have been computed as the sum of the absolute values of the errors that are introduced in the measurement of relative concentrations of HbO_2, HbCO and Hi due to a change in optical density measurements, as expressly required by dependent claims 11 and 29, and claims dependent therefrom. Öberg, ¶ 14; Nilsson, ¶ 14.

5. The rejections based on Brown *et al.* are wrong.

For the first time in the present application, the Examiner rejects claims in this application as being unpatentable over the teachings of Anderson *et al.* in view of Brown *et al.*, U.S. Patent No. 4,134,678. In light of the comments in the following subsections, Applicants respectfully traverse this rejection.

a. Brown *et al.* alters the blood sample by hemolysis.

The Brown *et al.* reference does not supply any of the discrepancies existing in the Anderson *et al.* reference, presented above in Section III.C.3. In particular, the Brown *et al.* reference presents multi-wavelength spectrophotometry which uses one wavelength for each blood component to be determined. Brown *et al.*, Figure 5; col. 3, lines 31-39; Schmitt 7/10/95, ¶ 16.

The only scattering correction contemplated by Brown *et al.* is accomplished by hemolyzing the blood sample before optical measurements are made. See Brown *et al.*, col. 6, lines 41-43; col.

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8, lines 2-4 and 21-22; col. 10, lines 8-9; col. 13, lines 55-68; col. 14, lines 16-17; col. 15, line 43; col. 16, lines 8 and 40; col. 17, lines 6 and 37; and col. 18, lines 9 and 36-37. Schmitt 7/10/95, ¶ 17; Mountain, ¶¶ 11, 13.

Thus, in striking contrast to the presently claimed invention, Brown *et al.* do not disclose or suggest the measurement of unaltered whole blood, and thus cannot supply the above-noted discrepancies in the Anderson *et al.* reference.

b. Brown *et al.* do not provide scattering correction.

As emphasized time and time again during the prosecution of this application, in accordance with independent claim 1 of the present application, the generation of a plurality of wavelengths is required, the plurality of wavelengths including an absorbance subset and a scattering subset. In particular, the Brown *et al.* reference uses one wavelength for each blood component to be determined (*see*, Figure 5 in col. 3, lines 31-39), and uses no other wavelengths. There is no disclosure or suggestion of scattering wavelengths, as required by the present invention. Schmitt 7/10/95, ¶ 16.

c. A co-inventor of the Brown *et al.* invention thinks the Examiner is wrong.

Charles F. Mountain is a named co-inventor of the Brown *et al.* patent. Filed herewith is the declaration of Mr. Mountain under 37 C.F.R. § 1.132, in which he refutes completely the Examiner's conclusion that the presently claimed invention would have been

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obvious in light of the combined teachings of Anderson *et al.* and Brown *et al.* Mountain, ¶ 12.

In particular, Mr. Mountain states that Anderson *et al.* do not present a practical system to determine concentrations of hemoglobin species in unaltered whole blood for several reasons. First, Anderson *et al.* require the measurement of optical density before and after hemolysis. Second, since light scattering may vary markedly from one clinical blood sample to the next, this would render the use of the Anderson *et al.* system to "correct" for scattering impractical. Mountain, ¶ 14.

Mr. Mountain also observes that the Brown *et al.* patent requires hemolysis prior to spectrophotometric measurements (Mountain, ¶ 11), and in the 28 years since the Anderson *et al.* paper was published, and in the 16 years since the Brown *et al.* patent was issued, all companies that have developed co-oximeters that measure total hemoglobin concentration produced instruments that hemolyze the sample before subjecting the sample to spectrophotometric analysis. Mountain, ¶ 15.

* * *

For these reasons, the rejection of claims based upon the teachings of Brown *et al.* should be withdrawn.

6. The rejections based on *res judicata* are unfounded.

The Examiner has concluded that claims 1, 2, 5, 6, 9-21, 23, 24, 26, 27 and 29-36 should be rejected under the doctrine of *res judicata* in light of the adverse decision in the appeal of parent application serial No. 07/313,911. Applicants respectfully

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traverse this rejection as presented in detail in the following sections.

a. *Res judicata* cannot apply because the issues are different.

The C.C.P.A. has consistently held that the doctrine of *res judicata* is only proper when the issues are the same. *See In re Herr*, 377 F.2d 610, 611 (C.C.P.A. 1967) (holding that if the specifications are materially different then the issues are different); *In re Fried*, 312 F.2d 930, 931 (C.C.P.A. 1963) (holding that if the claims are materially different then the issues are different). The Supreme Court stated this essential principle in *Commissioner of Internal Revenue v. Sunnen*, 333 U.S. 591, 597-98 (1948):

> The general rule of *res judicata* applies to repetitious suits involving the same cause of action. It rests upon considerations of economy of judicial time and public policy favoring the establishment of certainty in legal relations.

The C.C.P.A., stating the same essential principle, observed that "the issues must be identical before *res judicata* is applicable." *In re Fried*, 312 F.2d at 932 n.3. As shown below, the present case involves neither the same cause of action nor identical issues and *res judicata* was therefore improperly applied by the Examiner.

b. Different claims are different issues.

In re Fried addressed the impact of a difference in the claims between a parent application and a CIP application. The Board of Appeals had affirmed an examiner's rejection of a CIP based on *res judicata* from an earlier final rejection in the parent application. In reversing the Board, the court observed that "[t]o a person

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skilled in this art it is readily apparent that [the] claims ... of the parent application are broader than the appealed claims. ... The issue here is, therefore, a different issue than that decided [earlier]." *In re Fried*, 312 F.2d at 932; *see also In re Craig*, 411 F.2d 1333, 1336 (C.C.P.A. 1969) ("there exists sufficient technical ground for not applying *res judicata* in that the claims here on appeal are substantially different from the claims in the parent application").

In the present case, the claims in the parent application are, similarly, broader than the claims of the present CIP. For example, claim 1 of the present application is distinguishable from the corresponding claim 1 of application Serial No. 07/313,919. Claim 1 presently under examination requires the step of generating a plurality of radiation wavelengths, including an absorbance subset of wavelengths that has been selected by its ability to distinguish the constituent components and to minimize the effects of radiation scattering and to maximize radiation absorbance by the constituent components. Also included among the plurality of generated wavelengths is a scattering subset of wavelengths that has been selected to maximize the effects of radiation scattering by unaltered whole blood relative to the effects of radiation absorbance by unaltered whole blood. Claim 1 presently under examination also requires the calculation of concentrations of the plurality of constituent components, corrected for the effects of radiation scattering, based upon detected intensities of each of

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the plurality of wavelengths, including each of the absorbance subset of wavelengths and scattering subset of wavelengths.

In contrast, the claims on appeal in application Serial No. 07/313,919 required only the generation of a plurality of radiation wavelengths, without requiring a subset of those wavelengths to be an absorbance subset of wavelengths selected according to specified criteria, and without requiring a distinct scattering subset of wavelengths, selected according to different specified criteria. In addition, claim 1 on appeal in Serial No. 07/313,919 did not calculate concentrations of the constituent components as a function of all of the wavelengths including the scattering subset of wavelengths.

To further emphasize the distinctions between claim 1 presently under examination, and claim 1 on appeal in application Serial No. 07/313,919, Applicants, once again, present, in tabular form, the first and last elements of each claim.

FIRST AND LAST ELEMENTS OF CLAIM 1 UNDER EXAMINATION	FIRST AND LAST ELEMENTS OF CLAIM 1 ON APPEAL IN SERIAL No. 07/313,919
generating a plurality of substantially monochromatic radiation wavelengths, each wavelength of an absorbance subset of said plurality of wavelengths having been selected by their ability to distinguish the constituent components and having been selected to minimize the effects of radiation scattering and to maximize radiation absorbance by said constituent components, and each wavelength of a scattering subset of said plurality of wavelengths having been selected to maximize the effects of radiation scattering by unaltered whole blood relative to the effects of radiation absorbance by unaltered whole blood;	generating a plurality of radiation frequencies each determined to distinguish one said constituent component from another said constituent component, and to minimize the effect of radiation scattering and to maximize radiation absorbance by whole, undiluted blood;
calculating concentrations of said plurality of constituent components of said sample of unaltered whole blood corrected for the effects of radiation scattering, based upon detected intensities of each of said plurality of radiation wavelengths, and based upon predetermined molar extinction coefficients for each of said constituent components at each of said plurality of radiation wavelengths.	calculating concentrations of each of at least three said constituent components of said sample of whole, undiluted blood, based upon detected intensities of said radiation frequencies, and upon predetermined molar extinction coefficients for each of said constituent components at each of said radiation frequencies.

Since the claims of the CIP are narrower than those of the parent application, the issues are different and the doctrine of *res judicata* is not appropriate.

c. Different specifications are different issues.

In re Herr addressed the impact of a difference in the disclosures between a parent application and a CIP application. The court pointed out that the issue before it was whether or not

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the claims should be allowed in view of the application and record currently before the court. *In re Herr*, 377 F.2d at 611. The court then held that despite that "the present claims are identical to those sought to be patented earlier[,]" *Id.* at 612 n.5, the fact that the CIP contained additional disclosure and was supported by additional affidavits rendered the issues different. The court, therefore, held that *res judicata* was improper. *Id.* at 610-12.

In the present case, the CIP application contains additional disclosure relating to the selection of radiation wavelengths and the processing of the measurements to calculate concentrations of the constituent components of whole undiluted blood. In addition, as mentioned in Section III.C.1 above, ten declarations have been presented in the present case that were not in the record when the prior appeal was determined. Here, as in *In re Herr*, this information is directed to the discrepancies noted by the Board of Appeals when it rejected the parent application. The issues are, therefore, different and the application of *res judicata* is improper.

d. The issue was not actually and necessarily litigated.

"[W]here the second action between the same parties is upon a different cause or demand, the principle of *res judicata* is applied much more narrowly. In this situation, the judgment in the prior action operates as an estoppel, not as to matters which might have been litigated and determined, but 'only as to those matters in issue or points controverted, upon the determination of which the

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finding or verdict was rendered.'" *Commissioner of Internal Revenue*, 333 U.S. at 597-98 [citation omitted].

Although referred to as *res judicata* in *Commissioner of Internal Revenue*, the above-mentioned estoppel is commonly referred to as "issue preclusion." The Federal Circuit has crystallized the requirements for issue preclusion in *In re Freeman*, 30 F.3d 1459, 1465 (Fed. Cir. 1994):

> Issue preclusion is appropriate only if: (1) the issue is identical to one decided in the first action; (2) the issue was actually litigated in the first action; (3) resolution of the issue was essential to a final judgment in the first action; and (4) plaintiff had a full and fair opportunity to litigate the issue in the first action.

The second requirement is not satisfied in this case since the Board of Appeals, in its decision on the parent application, never addressed the question of whether the claims as modified in the CIP application would be allowable. The Board would have had to anticipate and reject the additional disclosure, the ten additional affidavits, the narrower claims of the CIP, and the extensive additional disclosure of the CIP. To the contrary, the Board's decision repeatedly stressed that the parent specification failed to disclose sufficient detail, implying that subsequent disclosures might remedy the omissions. See, Decision of the Board of Patent Appeals and Interferences, Appeal No. 92-0991 *passim*. It is this detail that the CIP application provides. In particular, the CIP application adds extensive disclosure relating to improving the calculation of the concentrations of the constituent components,

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including, for example, the correction of the calculation for the deleterious effects of radiation scattering.

Further, arguably these requirements could never be met in the present case. If the Board had anticipated the additional disclosure, the ten declarations and the narrower claims of the CIP, then the Board would have been addressing an issue that was not "essential to a final judgment" on the parent application. The third requirement would therefore be left unsatisfied and the Board's decision would not carry any preclusive effect.

e. *Res judicata* cannot stand alone.

If the other rejections are overturned, then the *res judicata* rejection cannot stand on its own. *In re Kaghan*, 387 F.2d 398, 401 (C.C.P.A. 1967); *In re Craig*, 411 F.2d 1333, 1336 (C.C.P.A. 1969); also *see* MPEP § 706.03(w).

MPEP § 201.07 provides, in pertinent part, for the right to file a continuation:

> The continuation application may be filed under ... 37 C.F.R. 1.62. ...
> At any time before the ... termination of proceedings on his or her earlier application, an applicant may have recourse to filing a continuation in order to ... establish a right to further examination by the primary examiner.

37 C.F.R. 1.197(c) provides that "[t]he date of termination of proceedings is the date on which the time for appeal to the court ... expires." For the parent application, that date was September 30, 1992. Since the present CIP application was filed on September 29, 1992, Applicants have established a "right to have that application examined." *In re Kaghan*, 387 F.2d at 401.

This right to an examination is not satisfied by a *res judicata* rejection. *In re Kaghan*, 387 F.2d at 401 ("holding of *res judicata* without reliance on any other ground of rejection is not an examination on the merits"); *see also In re Craig*, 411 F.2d at 1336 (quoting *In re Kaghan* with approval). The *Kaghan* court declared that the Patent Office had "waived [its] right to apply a *res judicata* rejection in these circumstances." *In re Kaghan*, 387 F.2d at 401. In these decisions, the C.C.P.A. seemed to be implying that if there are no other grounds for rejection (aside from *res judicata*), then the issues cannot be the same.

The *Kaghan* Court went on to declare that "[t]his analysis is completely consistent with MPEP 706.03(w)[.]" *In re Kaghan*, 387 F.2d at 401. Against the argument that the MPEP does not enjoy the force of law, the court reiterated its holding that "'the express provisions of MPEP set forth an established Patent Office policy on which applicants for patents are entitled to rely in good faith[.]'" *Id.* [citation omitted].

* * *

The issue in the present case is, as pointed out in *In re Herr*, whether the claims should be allowed in view of the application and record currently before the Patent Office. Both the claims and the specification are materially different in the present CIP application from those of the parent application, and substantial additional evidence supporting patentability has been introduced by declaration. Any one of these conditions alone would compel the conclusion that the CIP application and the parent

application present different issues; the fact that all three conditions exist only makes that conclusion stronger. Since the issues are different, the doctrine of *res judicata* cannot be applied. Moreover, if the other grounds for rejection are overcome, then it is not even necessary to address the merits of the *res judicata* rejection since it cannot stand on its own.

7. New claims 37-44 are also patentable.

a. Claims 37-44 are supported by the original specification.

Claims 37-44 are added by this paper. Claim 37 is independent, and claims 38-44 depend, either directly or indirectly from claim 37. As detailed in the exemplary citations to the specification below, each of these claims find support in the specification as originally filed, in compliance with 35 U.S.C §112, first paragraph. Although only these specific citations are provided, other support may exist.

Claim 37: page 20, line 24 through page 21, line 20.

Claim 38: page 20, line 24 through page 21, line 20.

Claim 39: page 21, lines 1-20.

Claim 40: page 20, line 14 through page 30, line 4.

Claim 41: page 30, line 14 through page 32, line 23.

Claim 42: page 16, line 12 through page 19 line 3.

Claim 43: page 26, line 19 through page 27, line 14.

Claim 44: page 26, line 19 through page 27, line 14.

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b. Claims 37-44 are patentable in light of the prior art.

New independent claim 37 requires the determination of k components of unaltered whole blood, by irradiating a sample of unaltered whole blood with n radiation wavelengths, k of the n wavelengths having been chosen to measure absorption by the k components, and the remaining n-k wavelengths having been chosen to compensate for the effects of scattering factors in the unaltered whole blood. As emphasized above, none of the prior art measure unaltered whole blood, and none use additional radiation wavelengths to compensate for scattering factors. Dependent claims 38-44 are also patentable for these reasons, and for the additional detail recited therein.

Specifically, there is no suggestion in the prior art of record for the calculation of the concentrations of the k components using a set of n linear equations that equate a vector of n optical densities with a linear combination of k light absorbance vectors and n-k light scattering vectors, as required by new dependent claim 38, or for each of the k light absorbance vectors corresponding to a specific one of the k constituent components, the entries of each light absorbance vector being extinction coefficients of a corresponding constituent component at each of the n wavelengths, as required by new dependent claim 39.

In addition, the prior art of record does not disclose the iterative determination of scattering vectors as functions of the composition of the unaltered whole blood sample under analysis, as recited in dependent claims 40 and 44.

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There is no suggestion in the prior art of record for the correction of the calculated concentrations of the k constituent components for the effects of finite spectral bandwidth of the n wavelengths, as required by new dependent claim 41, or for the correction of the calculated concentrations of the k constituent components as a function of the relative concentrations of the k constituent components, as required by new dependent claim 43.

Finally, the prior art of record does not contemplate the selection of four radiation wavelengths by computing an error index for each of HbO_2, HbCO and Hi as the sum of the absolute values of the errors that are induced in the measurement of relative concentrations of HbO_2, HbCO and Hi due to a change in optical density measurements, and the selection of a quadruple of radiation wavelengths having minimum error indices, as required by new dependent claim 42.

IV. CONCLUSION

Applicants believe the foregoing to be a full and complete response to the outstanding Office Action. The issuance of a timely Notice of Allowance for claims 1-44 is respectfully requested. Should the Examiner believe that another personal discussion would be helpful, she is invited to contact the

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undersigned attorney at (512) 418-3005 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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